In specific response to the applicants submission of March 18, 2002, the examiner stated that Battistini '149 "shows a very little amount of pre-swollen starch (10 grams out of 415 grams)." The examiner also asserted that Battistini '149 discloses starch as a diluent, as a disaggregating agent and also as a binding agent. Therefore, the examiner opined that the remainder of the starch (405 grams) could have been used as a dry binder. The examiner the went on to state that claims 1-3 have again been rejected because the amounts of the ingredients are not defined in the claims. The applicants respectfully traverse.

As those of skill in the art will understand (and the examiner may not), the term pre-swollen starch is used to indicate that a certain fraction of starch has been hydrolyzed to molecules of a lower molecular weight. Starch has a very high molecular weight, and therefore, normally neither dissolves nor swells in water. However, if a part of starch is hydrolyzed, it does become partially water soluble and swells in water. This is what happens when we add starch to our food and heat to make, for example, a thick gravy (heat hydrolysis starch).

Based on the above information, those of skill in the art will also readily recognize that the starch in Example 17 of Battistini '149 is pre-swollen. Specifically, corn starch is being added to warm water prior to use to hydrolyze the starch, allowing it to swell. Further, Battistini '149 states that "the resulting paste is used...," which locks in fact that part of the starch is pre-swollen. It is also important to note that the process of pre-swelling is irreversible (once lower molecular weight starch forms, it cannot revert back to the higher molecular weight molecule). Therefore, any final product will contain pre-swollen starch as well.

As the examiner should be aware, a claim is anticipated only if each and every element is described in a single prior art reference. As stated numerous times before, the applicants' claimed tablet composition does **not** contain pre-swollen starch. As admitted by

the examiner (in the final official action), Example 17 of Battistini '149 shows the use of pre-swollen starch. Given that important distinction, the cited U.S. patent **cannot** possibly anticipate claims 1-3 of the present application. Thus, applicants are at a complete loss as to why the examiner continues to improperly reject claims 1-3 under 35 U.S.C. §102(e) over Battistini '149

With respect to the examiner's comments that the present rejection is maintained over claims 1-3 in that "the claimed amounts of the ingredients are not recited in the rejected claims," the applicants fail to note the relevance to the present rejection. The applicants submit that the examiner has merely made the statement without any support in fact whatsoever and further submit that the statement is wholly unrelated to a rejection based upon an alleged lack of novelty.

Because the cited document does not specifically exclude the use of pre-swollen and in fact uses pre-swollen starch, the applicants submit that the claimed invention is **cannot** be anticipated by Battistini '149. Therefore, the applicants respectfully request that the rejection of claims 1-3 under 35 U.S.C. §102(e) be withdrawn.

Claims 1-6 were rejected under 35 USC § 103 as being unpatentable over to Battistini '149 in view of U.S. Patent No. 5,593,691 (hereinafter Eugster '691. As before, it is the examiner's position that it would have been *prima facie* obvious to modify the table of Battistini '149 using the ingredients in view of the teaching of Eugster '691). The applicants traverse.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success.

Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The primary document cited by the examiner, Battistini '149, simply neither teaches nor suggests all of the claim limitations of claims 1-6. Specifically, the applicants teaches the unambiguous exclusion of pre-swollen starch. Battistini '149 teaches the inclusion of pre-swollen starch. The applicants' cannot be any clearer on this point.

The examiner cited Eugster '691 to overcome the deficiencies of Battistini '149. Eugster '691 teaches new biotenside esters for use in the preparation of spontaneously dispersible concentrates containing therapeutic or cosmetically active substances (col. 1, lines 7-10). Eugster '691 teaches that cyclophosphamide may be combined with these esters. *See* Eugster '691 at column 11, lines 55-56. Eugster '691 also teaches that the sterol esters disclosed therein may be incorporated into conventional pharmaceutical preparations, together with customary excipients and/or diluents and stabilizers. Eugster '691 neither teaches nor suggests that applicants claimed invention.

The examiner again stated that "exclusion of preswollen starch does not impart patentable distinct [sic], since the prior art obtained the same results desired by applicants, *i.e.*, a coated tablet containing phosphamide having excellent stability and bioviability." The applicants strongly disagree with this statement. First of all, exclusion of a claimed component, pre-swollen starch, must be motivated by the teachings of the cited references. No motivation is provided by either reference to modify the hypothetical tyrosine kinase/cyclophosphamide compositions of Battistini '149 to comprise a tablet that does not contain pre-swollen starch. It is the applicants finding, and not that of the cited documents, that exclusion of specific starches provides improved stability of the compositions containing phosphamides. The applicants have shown that exclusion of pre-swollen starch results in unexpectedly improved stability of cyclophsphamide and reduced discoloration of the

disclosed compositions. See Table on page 3, especially examples 9 and 10. These results could not have been expected from the teachings of the cited references alone or in combination.

In view of the foregoing, Battistini '149 either alone or in combination with Eugster '691 neither teaches nor suggests the applicants' claimed invention and thus the examiner has failed to establish a *prima facie* of obviousness. Therefore the applicants request that the rejected under 35 U.S.C. §103(a) be withdrawn.

In view of the foregoing remarks, the applicants respectfully submit, again, that the application is in condition for allowance. Notification to that effect is respectfully requested. Should any questions relating to patentability remain, the examiner is **strongly urged** to contact the undersigned at the number indicated.

Respectfully submitted,

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